ChemistryNL

Roadmap

Chemical Sensing & Enabling Technologies

ChemistryNL

Contents

Introduction

Creating ultimate insight into and understanding of chemical composition and molecular processes is crucial to the development of revolutionary technologies such as personalized diagnostics, circular manufacturing, enabling the 'factory of the future' and utilizing sunlight as primary energy source. With the Chemical Sensing & Enabling Technologies (CSET) roadmap, ChemistryNL lays out the developments necessary to achieve the spatial and temporal resolution of chemical identification and quantification and the fundamental chemical understanding of molecular processes that is indispensable for the development of novel technologies. Given the broad applicability of CSET, developments in this field will enable breakthrough innovations in many sectors and industries, thus contributing significantly to the realization of solutions for various societal challenges.

The CSET roadmap is intended to help researchers clarify to what extent their open innovation project proposal may contribute to the further advancement of CSET as a technology field, while contributing to the development of solutions for societal challenges in relevant application areas. The programme council will use the roadmap as a guideline to assess the eligibility of project proposals submitted to ChemistryNL in the CSET domain.

The CSET roadmap aims to align public-private research, development, and innovation projects funded by ChemistryNL to the central missions underlying the Dutch Topsector innovation policy. For the preparation of this roadmap, the CSET programme council has based itself on the various Knowledge and Innovation Agendas (KIAs), https://www.topsectoren.nl/missiesvoordetoekomst, which have been prepared by the various Topsectors together with public and private partners for the period 2024-2027. As a result, the roadmap is organized in six chapters according the themes addressed in the KIAs/IKIAs:

- Agriculture, water and food
- Climate and energy
- Circular economy
- Digital chemistry
- Health & care
- Industrial safety and process development (as a CSET adaptation to the KIA safety)

For each KIA, the topics with a relevant link to CSET have been identified. Based on this matching between (KIA) application areas and (CSET) technology areas, specific tasks, goals and ambitions have been defined for the CSET-related developments for each KIA in the coming years. These are described and elaborated in the separate chapters of this roadmap.

In addition to the already mentioned KIAs, the programme council CSET has established that there is strong overlap between many CSET-related technologies and the KIA Key Enabling Technologies (KETs). Since a large majority of these technologies and the needed technological advances are already covered in the above-mentioned thematic chapters, it was decided not to include a separate chapter on KETs in this roadmap in order to avoid too much redundancy. The CSET council furthermore underlines the importance of the National Technology Strategy (NTS) for CSET-related technological advances, https://www.rijksoverheid.nl/documenten/beleidsnotas/2024/01/19/de-nationale-technologiestrategie. The following eight technologies, that have been elected amongst the ten priority technologies, are relevant for the chapters in this roadmap:

- Optical systems and integrated photonics
- Process technology, including process intensification
- Biomolecular and cell technologies
- Imaging technologies
- Mechatronics and optomechatronics

- Artificial intelligence and data science
- Energy materials
- Semiconductor technologies

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March 2025

1. Agriculture, Water & Food

Introduction

To provide the future world population with sufficient, and healthy food products, and safe water, the way that agriculture and water production are currently carried out needs to be rethought in such a way that the impact on our planet is reduced and ideally minimized, therewith adding to resilience. For example, of all the energy used on earth, ~30% is used to produce food, and of all the potable water >70% is used in food production. What is maybe even more shocking is that globally 35-50% of the food is wasted of which in general one third is created in households. Besides, there is an imminent climate effect in the choices made for ingredients; e.g. animal based proteins have ~ 10 times higher impact on our climate compared to their plant-based counterparts. Furthermore, water availability and quality is becoming more and more of a worry due to increased prevalence of e.g. components related to medicine usage, and the very high demand that food production has on the available potable water. In order to mitigate this, advanced nanofiltration techniques need to be developed to thus contribute to many of the UN sustainability goals.

Within this roadmap, we target (food)materials, processes, devices and systems that make food and water production intrinsically more sustainable, reliable, and safe. Just to name a few: advanced sensing technology to allow precision nutrient as well as herbicide dosing to agricultural crops either in the field, green houses, vertical farms, etc. Sensors for the real-time monitoring of critical molecular parameters. The sensors will enable closed-loop control for sustainable food production and processing in different food chains. Temperature sensors that allow food production systems to enhance food quality, and reduce food waste. High-tech separation devices that facilitate production of effective raw materials (e.g. to facilitate the protein transition) or warrant water quality (and effective removal of e.g. pharmaceutical residues). Devices that allow high-throughput screening of ingredient functionality to speed up food product design, as well as analyze human digestion (e.g. using highly advanced sampling pills) and elucidating health effects that food has on humans, e.g. in combination with organs-on-chips to test the effect that nutrients have on organs. These three last points will be the stepping stone toward personalized nutrition directed at creating health effects. A special point of attention is toward zoonotic diseases that are very much linked to food, and for which currently various techniques are under development.

In all attention points, the use of nano/microtechnology is essential because the determining factors act on nano- and micrometer scale, which can uniquely be assessed by these technologies.

Figure 1: *Agriculture, Water & Food topics covered in this chapter.*

Considering the relevance of agriculture, food, and water for our future, this chapter is divided into the three tasks shown in Figure 1. An overview of the short-term, medium-, and long-term goals within each task is provided in Table 1.

Table 1: *Agriculture, Water & Food tasks and their goals.*

Task	Short term goals now – 2030	Medium term goals 2030 – 2035	Long term goals 2035 – 2040	Ambition
Water purification and safety	• Advanced (membrane) separation, and hybrid technologies that allow specific removal of medical components. • Separation devices with uniform pores in the (sub-)nanometer range, and anti-fouling properties that allow them to operate in tandem with microbial water treatment methods.	• Innovative separation concepts directed toward removal / destruction of antibiotics/antimicrobial components to thus reduce resistance issues.	• Integrated water treatment systems directed to affordable and inherently safe potable water for all.	NL will be a major player in highly automated water treatment concepts
Sensors for agriculture	• Low-cost, micro-spectrometers in the VIS-NIR and SWIR spectral ranges (price reduction: factor 10, production volume increase: factor 100). • Sensors for Nitrogen compounds to support decisions on farming/construction and travel.	• "Intelligent spectrometry" with embedded data analysis for rapid alert. • Large scale distributed sensor networks to monitor critical parameters in various environments	• Low-cost, micro spectral-imaging in the VIS-NIR, SWIR and MIR spectral ranges (price reduction: factor 100, high-volume production: > Mio units/years).	NL will be a major player in development of sensors for driver for AI-enabled discovery of new and sustainable molecules and materials
Microfluidic devices and sensors for food production and nutrition	• Highly efficient and sustainable food production lines make use of advanced sensing using micro- and nanotechnology. • Sensors will first be used at-line (taking individual samples) and thereafter on-line (continuous sampling and measurement).	• Food products designed based on ingredient functionality, making flexible use of starting materials complying with circular economy principles.	• Personalized food products and additives directed toward improving individuals' health • Integrated food concepts that	NL leads innovation in healthy food production, minimized food waste, and sustainable food production from ingredient, energy and

			can be prepared on demand,	water usage. This will add healthy years to peoples' lives, and reduce dependency on health care.

1.1 Water purification and safety

In order to make the Dutch water systems robust (management of scarcity as well as abundance of water), and safe (free of contaminants), advanced monitoring and separation methods are needed. Specifically the prevalence of pharmaceutical residues is becoming more and more of an issue, since these components can be hormonal in nature, and thus affect wild life (in e.g. our rivers), and also humans if present in our drinking water (e.g. having effect on birth control). Furthermore, the presence of antibiotics will impact water purification plants as we know them, since the micro-organisms that are applied are affected by it, and also some species may become resistant to antibiotics leading to potential health threats.

Sustainable separation technology

It is of greatest importance to develop advanced separation technologies that target health-threatening components, such as pharmaceuticals, but maybe even more importantly also adjust the mineral content to prevent e.g. silting of the soil. For this, advanced separation technologies are needed, that are not only relatively low in energy usage, but also in chemical use, and can be applied on very large scale. This may imply that various methods need to be used in hybrid or cascaded fashion. This is only possible if highly advanced sensing technology can be applied to steer the various product flows, and this not only creates water that is safe to use, but also limits environmental effects (ranging from disposal of the concentrate, to energy use, and chemical use). A method that could match these requirements is membrane filtration that can be applied for various separations relevant to water (and also to food ingredient preparation).

Development of separation technologies

In the field of membranes, various filtration techniques are available, and when used in tandem they can achieve the previously described requirements. Still, improvements compared to the current state of affairs need to be made to make this future proof. Part of that improvement is on the characteristics of the membranes, the processes used to make them, as well as the processes in which they are applied. In all cases, advanced sensing technology will be of the essence to steer technology at a higher level than is currently available. For the membrane characteristics this implies preparation of better defined and more uniform pore sizes, in membrane production this implies the use of materials and processes that are inherently more sustainable (reduced / no solvent use, considering end-of-life options for membrane modules), and in membrane processes, making better use of the combined effects that can be created by using membranes in conjunction. For this to work optimally, and also flexibly in regard to the incoming flow composition, advanced sensing tools are needed, both for chemical composition monitoring (with as a big challenge measuring very low concentrations), as well as registering process conditions. It is expected that artificial intelligence will become more and more instrumental in creating this.

Future perspectives

The principles that are developed within the field of water purification can be applied to other fields as well, e.g. food, pharma, biorefineries etc. It is expected that further tailoring would be needed, e.g. to control affinity of molecules with the separation device. This can be both to prevent as well as to steer them to be more strong, as well as to be broken upon a trigger. In that sense, electrically driven processes are expected to become relevant since they are low in energy usage, and can be highly effective, either attracting / repelling components, as well as locally changing conditions through electrode reactions (e.g. water splitting) thus reducing chemical usage.

1.2 Sensors for agriculture

The Netherlands have a long standing tradition in agriculture and food. Current food production practices have a huge impact on the world we live in regarding energy and water used, for example, as mentioned in the introduction of this chapter, and we are also in a position to improve on this, given the high level of technical knowledge available in our country. Extensive use of sensors can be applied to monitor primary production, as described in this section, as well as production of food, and food ingredients as described in the next section. More and more diagnostic tools to monitor critical elements in the (bio)chemical compositions of water, air, soil, biological tissues, packaging and waste are available. Target areas are amongst others animal health monitoring, food, feed & beverage safety (microbial contamination management, pesticide, agrochemical, veterinary drugs), air, water and soil quality measurement (contaminants). Furthermore, also through the development of vertical farming, plant health can be monitored at a many different levels (chlorophyll, water, nutrition), thus contributing to step-wise efficiency increase.

Safety aspects related to primary production

As is the case with the world as a whole, the contamination of the environment in an agricultural setting is a great concern for global health. Besides, it may lead to potential epidemics caused by existing, new and emerging infectious diseases (including from antimicrobial-resistant pathogens, and zoonotic origin), placing a burden on health and veterinary systems, reducing consumer confidence in food, and negatively affecting trade, food chain sustainability and food security. Many of the infections are zoonoses, necessitating an integrated, cross-border, "one health" approach to research and public health measures in the human and veterinary field, including the food chain. The European RASFF (The Rapid Alert System for Food and Feed) program is an example of a program that addressed these hazards, for which the spectroscopic techniques are highly relevant. To lead to the functionality that the current challenges are asking for, spectroscopy requires compact and robust devices which can be produced at high volume and low cost. For this, miniaturization is the way to go, to ultimately also address the need for real-time measurements.

Miniaturization and affordability of the measurements

Some optical spectrometers are versatile and compact, but better mobility and robustness, and further miniaturization will allow more applications in the field. The effects of miniaturization are threefold. Firstly, small spectrometers enable local measurements in confined environments and these can be configured as an array of sensors in a network. Secondly, small spectrometers are portable and can therefore be used on the spot anywhere where needed. Finally, small devices open the door for drastic cost reductions and volume production. These three effects reinforce and will create new volume applications and markets.

1.3 Microfluidic devices and sensors for food production and nutrition

Chemical and biochemical research increasingly exploit the use of microfluidic devices and sensors for the detection and synthesis of compounds, and for tailoring formulations, to thus maximize the effectivity of compounds. Compared to that the use of such technologies are not that widespread in food production. In post-harvest processing, sensors with molecular precision will enable the real-time monitoring of critical molecular parameters, which will allows for closed-loop control to enable sustainable food processing in different food chains. Furthermore, as is the case in chemical industry, process control is becoming more elaborate thanks to extensive sensor usage, leading to cost-effective means to increase product quality levels, reduce waste, reduce energy, and to increase safety of existing and new production methods. Besides, it is expected that e.g. micro-technologies will be instrumental in synthesis of small amounts of high-value specialty products, as well as allow controlled structure formation, relevant for food. Such technologies especially when applied in high-throughput screening fashion, will speed up upscaling from research to production as has been demonstrated in 'scalable flow chemistry'.

Ingredient functionality testing

The development of microfluidic techniques for functionality testing (e.g. the stabilization of small droplets and bubbles) is an important step to make the use of ingredients much more flexible. This will not only help innovations in food design, but also contribute to the protein transition. To replace animal-based proteins with their plant-based counterparts (one of the primary sustainability targets of the Dutch government), it is essential that functionality of these components can be tested on small scale, to allow for fast product formulation and development. The small scale points toward the device that needs to be able to make small structures, as well as a device that can be operated when only small amounts of an ingredient are available, thus boosting food design.

Functionality testing can also be extended toward digestion. If digestion of foods is understood better, and the local release patterns of digestion product is knows, this would explain health effects that certain foods create, or are detrimental to our health. There are encouraging developments that allow both structure degradation, as well as component analysis on chip. Furthermore, there is a clear link with the previously addressed organ-on-a-chip applications, that may be considered as a next step to connect the properties of a food or medicine to effects created in the body. As such these devices will allow us to either eat, or keep ourselves healthy at a level that is currently unheard of, and add healthy years to our lives. Sampling pills as are currently developed will be instrumental in monitoring whether the anticipated effects as take place in humans.

Food safety

Contamination management is crucial in food safety, and thus is early detection to prevent any spoilage and dangerous situations down the line. The interval between preparation of a food and detection of a microorganism needs to be reduced, from several days, to minutes or, at most, hours, to prevent re-calls. Spectroscopy is an ideal technology for this because sample preparation is minimal and results are available within seconds to minutes. Because food production is expected to become more circular, this detection is expected to become even more relevant because of increased risk of reintroduction in the production chain. Besides spectroscopy, pathogen detection methods include biosensors, such as electrochemical biosensors, piezoelectric biosensors and thermal biosensors.

Another illustrative example relevant to both food and medicine is the use of sensors on individual products to monitor the quality of the content; this would take us into a new realm in which the 'good to be used until date' will be replaced by an indicator that directly indicates whether a product is safe to use, and thus greatly prevent food waste. In order to make this a reality for food, such sensors would need to be cheap, and biodegradable to prevent plastic waste.

1.4 Multi-disciplinary approaches

The development of the previously mentioned devices requires a crossover between partners in micro/nano-technology, chemical and food synthesis, and biomedical sciences, with a key role for innovative high-tech SMEs. In The Netherlands, many micro/nano and biotech SMEs have emerged, backed by world-renowned research groups at universities/institutes. Scientifically, microfluidic technologies are to be developed for the synthesis of new formulation concepts (e.g. foods, encapsulates, and so on) as well as devices that can be applied to monitor digestion. Industrially, the added value of food can be improved while producing it more effectively, and food products may even become personalized. A positive image of food in society can be achieved by focusing on sustainable and environmentally friendly food products, such as plant-based proteins, fermentation-based production, meat alternatives, and allergen-free, or more in general, safe food products. It is within reach to achieve sustainable food production processes with intrinsic health benefits for consumers by making use of the advanced technological developments that are currently taking place, and are expected to become a reality in the near future.

2. Climate and Energy

2.1 Introduction

The Netherlands has a legal climate goal of a 55 % reduction in greenhouse gas emissions (GHG) by 2030, and the aim is even higher at 60 % reduction by 2030 and ultimately climate neutrality by 2050. In the recently published Climate and Energy Outlook of the Netherlands (KEV) [1], it is reported that with current implemented policy we are heading for a reduction of 44-52 % in 2030, compared to 1990 levels. The KEV furthermore concludes that additional policy with rapid effect is needed to bring climate goals back on track. The current Integrated Knowledge & Innovation Agenda (IKIA) for Climate & Energy contains 16 missions and multi-year innovation programmes that together form the backbone of the overall 2024-2027 plans towards the energy system of the future. These are divided into the following categories:

Mission	Theme
A	Electricity
B	Buildings & Infrastructure
C	Industry
D+	Mobility
E	Agriculture
other	System integration, nuclear energy

Developments and deployments in analytical characterization tools, (chemical) sensing/monitoring systems and enabling technologies will be important or even crucial for reaching the goals in many of these missions. The required CSET developments have been divided into the three themes shown in Figure 2, which are further detailed in sections 2 - 4. An overview with examples of short-term, medium-, and long-term goals within each theme is provided in Table 2.

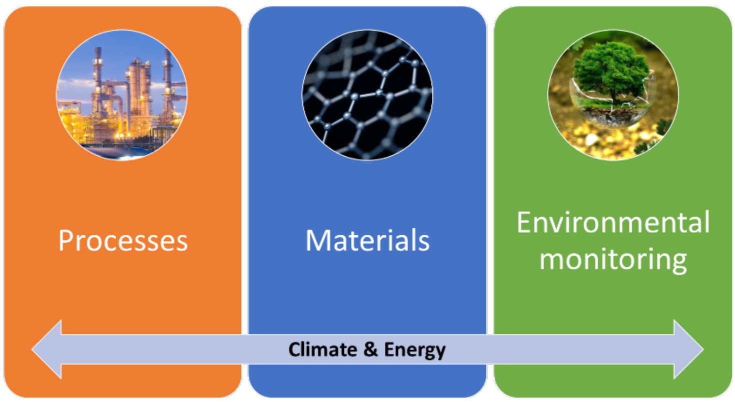

Figure 2: *Climate & Energy themes covered in this chapter.*

Table 2: *Climate & Energy tasks and their goals.*

Task	Short term goals now – 2030	Medium term goals 2030 – 2035	Long term goals 2035 – 2040	Ambition
Processes	• Sensors and AI/ML for electricity grid optimization • Advanced sensing technologies for CCS, renewable energy storage, biofuel and H_2 production	• Implementation of advancing sensing in large-scale industrial and energy projects	• Integrated advanced electrochemical sensing and data analytics into energy systems	Achieve global deployment and integration of advanced sensing technologies for climate and energy management.
Materials	• Sensors for monitoring electrolyte composition in flow batteries • Sensors for optimizing hydrogen fuel cell performance	• Automated inspection systems for buildings • Sensors for monitoring battery health and degradation factors in energy storage systems • Analytical and sensing contributions to new materials (photovoltaics, solid-state batteries, catalysts)	• Develop key enabling technology involving, among others, analytics/sensing and AI for new-generation materials discovery	Large-scale leverage of analytical, sensing, and AI tools to discover, develop and deploy materials for climate and energy applications
Environmental monitoring	• Sensors and sensing for UFP concentrations and chemical content • Methodologies for health relevant indicators • Monitoring methods based on molecular biology	• Real time sensor networks for chemical pollution, health relevant indicators and ecosystems	• Real time sensor network redout is used for dynamic management and optimization for human and environmental health	Using monitoring networks to optimize transitions and promote, human, and environmental health

2.2 Processes

The energy transition and sustainable (chemical) production rely to a large extent on the development and upscaling of new or improved processes, including the electrolytic production of hydrogen, electrochemical reduction of CO_2 into valuable chemical building blocks, the switch from fossil- to biobased raw materials, and the development of new (bio)catalytic processes. CSET-relevant tasks in this theme are exemplified in Table 3.

Table 3: *CSET-relevant tasks in the theme Processes.*

Task	Examples
Electricity	Sensors capable of real-time monitoring of voltage, current, and power quality. These sensors will be integrated into fault detection and predictive maintenance systems to prevent power outages and enhance grid performance.
Electrochemistry and -catalysis	Innovations in sensors for monitoring electrolyte composition in flow batteries and optimizing hydrogen fuel cell performance. These sensors will contribute to the efficiency and reliability of renewable energy storage systems; Novel characterization tools for studying (electro-)catalytic processes *in operando*.
Hydrogen	Sensors for monitoring the safety, infrastructure, and transport of processes involving H_2.
Biobased chemicals and biofuels	Real-time microbial activity sensors to monitor fermentation processes in biofuel production. Additionally, sensors capable of analyzing the chemical composition of biomass feedstocks are needed to optimize biofuel production processes.

2.3 Materials

In addition to new or improved processes as described in section 2.2, the IKIA for Climate & Energy also requires the development of new or improved materials for applications in batteries, fuel and solar cells, electrolyzers, etc. Examples of CSET-relevant tasks for research and development of such materials are provided in Table 4.

Table 4: *CSET-relevant tasks in the theme Materials.*

Task	Examples
Batteries	Analytical characterization tools for R&D of (flow) battery innovations
Electrolysis	Analytical characterization tools for R&D of new electrolyzer systems (e.g. for electrolytic production of H_2)
Photovoltaics	Analytical characterization tools for R&D of improved photovoltaic materials with optimum optical, electronic and chemical properties.
Buildings	Automated inspection techniques

2.4 Environmental monitoring

Environmental monitoring plays a vital role in supporting the energy transition while addressing the interconnected challenges of climate change and public health. Advanced sensing technologies and environmental modeling are key to managing transitions in an optimal manner for ecosystem and human health. Examples of CSET-relevant tasks in the theme Environmental monitoring are provided in Table 5.

Table 5: *CSET-relevant tasks in the theme Environmental monitoring.*

Task	Examples
Air quality	Sensors and sensing for: • Emissions and leaks: H_2, CO_2, nitrogen compounds, methane • Volatile organic compounds (VOCs) • Fine particulate matter
Water and soil quality	Sensors and sensing for: • Emission of pollutants in industrial waste water • Nitrogen compounds • PFAS • Drugs (waste) and degradation products • Micro- and nanoplastics
Remote sensing	Lightweight, high-resolution sensors on satellites and unmanned aerial vehicles (UAVs) to monitor atmospheric composition and greenhouse gas concentrations on a global scale.
Sensing networks	Sensor and sensing grids for air and water quality monitoring, ecosystem state (eDNA), climate data collection, urban environments. The resulting data streams are used for holistic modeling, digital twinning, prediction purposes and generating advice with impact.

2.5 References

[1] Klimaat- en Energieverkenning 2024, Planbureau voor de Leefomgeving publicatienummer 5490, October 2024.

3. Circular Economy

3.1 Introduction

The circular economy (CE) is an economic system aimed at reducing waste and continually (re-)using resources. Unlike the traditional linear economy, which follows a 'take, make, dispose' model, the CE focuses on reusing materials, reducing waste, and designing products for longer lifecycles. This approach conserves resources, reduces environmental impact, and enhances sustainability. The urgency to create a CE is driven by the need to address resource scarcity, environmental degradation, and climate change.

The CSET council's roadmap aligns closely with Dutch and EU CE strategies. The Dutch National Circular Economy Programme 2023-2030 [1] and the EU Circular Economy Action Plan [2] provide frameworks for transitioning to a CE, and consider it as a key component of achieving climate neutrality by 2050 and halting biodiversity loss. These policies emphasize the Safe and Sustainable by Design (SSbD) [3] framework, ensuring products are designed with safety and sustainability from the start. Horizon Europe goals further support these initiatives by funding research and innovation in CE practices. The Knowledge & Innovation Covenant (KIC) 2024-2027 supports CE initiatives by focusing on societal challenges and promoting interdisciplinary collaboration and innovation within KIA Circular Economy [4] and KIA Key enabling technologies [5]. Additionally, the focus on critical raw materials highlights the potential to improve recycling and reuse, reducing dependency on imports, supporting sustainability and strategic goals.

By aligning with these policies and leveraging advanced technologies, this roadmap promotes advances to the CE, speeding chemical industry transitions by developing tailored advanced sensing and monitoring technologies. These technologies will enable efficient resource use, better waste management, and the creation of sustainable materials chains, ensuring that (chemical) processes and products are both safe and circular, see Figure 3. An overview with examples of short-term, medium-, and long-term goals within each theme is provided in Table 3.

***Figure 3**: Circular Economy topics covered in this chapter.*

Table 6: *Circular Economy tasks and their goals.*

Task	Short term goals now – 2030	Medium term goals 2030 – 2035	Long term goals 2035 – 2040	Ambition
Sensing and Monitoring Technologies for Circular Processes	• Develop and deploy real-time sensors and analytical tools for resource efficiency and waste stream analysis.	• Scale sensing and monitoring systems across industries for integrated real-time process control.	• Achieve fully autonomous sensing systems across industrial sectors for closed-loop resource efficiency.	Position the Netherlands as a global leader in advanced sensing technologies that optimize circular chemical processes.
Innovative Materials and Recycling Technologies	• Develop advanced analytical techniques for sorting and recycling. Applications demonstrated in pilot projects and plants.	• Scale advanced recycling and material recovery sensing technologies to handle diverse material streams.	• Develop fully autonomous recycling systems that achieve full material recovery and enable seamless circular production cycles.	Lead in sensing and analytics for sustainable material innovation and high-efficiency recycling technologies
Safe and Sustainable by Design (SSbD) sensing needs	• Clarification and standardization of SSbD sensing needs. • Analytics developed for SSbD circularity. • Sensing and screening analytics implemented in SSbD R&D projects.	• SSbD requirements standardized and platforms developed for in depth analysis as well as screenings. • Automated screening and sensing implemented in SSbD R&D projects	• Fully autonomous SSbD fit screening and sensing implemented in relevant stages of a product life cycle.	Facilitate the successful uptake of SSbD by providing the approaches and data required for data driven decision making.

3.2 Sensing and Monitoring Technologies for Circular Processes

Achieving a circular economy demands precise tracking and optimization of material flows, waste streams, and resource use. Sensing technologies are crucial in providing the real-time data necessary to drive these improvements. However, integrating these systems into industrial processes and managing the vast data they generate are significant challenges. The following subsections explore specific areas where these technologies can enhance circular processes, while addressing the technical hurdles industries face.

Real-Time Monitoring

Real-time monitoring of (chemical) processes ensures that resource use is optimized and waste is minimized. However, the costs and complexity of implementing these systems at scale, combined with the challenge of processing and interpreting data in real-time, limit their widespread adoption.

Many industries struggle to integrate these systems into existing processes and manage the vast amounts of data generated, which limits their ability to maximize resource efficiency. For optimal results, real-time monitoring systems should be integrated into the design phase of any new project, rather than being added once a process is operational.

Waste Stream Analysis

As industries introduce new materials and processes, waste streams are becoming more complex, requiring advanced analytics to accurately characterize them. Traditional methods often lack the selectivity or sensitivity to detect and identify a wide range of compounds, particularly from novel materials like bio-based polymers or advanced composites. In-depth analysis is crucial for assessing the recyclability and valorization potential of these complex waste streams. Such detailed understanding is necessary to recover valuable materials and convert waste into usable resources. As chemical processes evolve, continuous monitoring and real-time analytics are needed to adapt to shifting waste compositions, ensuring both efficient resource recovery and proper management of contaminants in line with circular economy goals.

Life Cycle Assessment (LCA) Integration

Although chemical sensing and analytical data provide critical information for understanding material flows and process efficiency, these insights are often disconnected from traditional LCA models. This gap makes it difficult to leverage real-time data for assessing the environmental impacts of materials and processes in a holistic way. To achieve better alignment between LCA and real-time monitoring, more cohesive data integration is needed. Emerging AI-driven approaches for new material development can help address this challenge by automating the linkage between chemical sensing data and LCA frameworks. Monitoring of material degradation state or life time, coupled to (preventive) maintenance, could extend the use of a product and prevent premature recycling.

Catalyst Development for Circular Processes

Catalysts are critical for enabling efficient (chemical) processes, especially when using circular feedstocks like recycled or bio-based materials. Circular feedstocks can introduce impurities or inconsistencies that can disrupt catalyst performance, making the development of robust monitoring tools essential. Sensing technologies and real-time analytics are crucial for monitoring catalyst activity and ensuring optimal performance. These tools provide real-time data on catalyst conditions and reaction environments, allowing for dynamic adjustments to maintain efficiency, even as feedstock composition changes. Incorporating such technologies into new catalytic processes ensures better resource utilization and reduces waste, supporting the scalability of circular feedstock integration into industrial operations.

Sensing and Analytics for Critical Raw Material Recovery and Substitution

The recovery and substitution of Critical Raw Materials (CRMs) are central challenges in the circular economy. Advanced sensing technologies are essential for identifying and separating CRMs from complex waste streams, enabling efficient recovery of valuable materials. Integrating design for recycling from the outset ensures that products are engineered to facilitate the recovery of CRMs at the end of their lifecycle. Sensing also plays a key role in sorting, improving the separation of CRMs from contaminants during recycling. By incorporating these sensing systems early in the design process, industries can enable in-line monitoring for sorting and recovery, optimizing CRM reuse and reducing resource dependency where CRM substitution is unavailable.

3.3 Innovative Materials and Recycling Technologies

Developing innovative materials and recycling technologies is essential for advancing the circular economy. However, there is a delicate balance between designing materials that fit within existing infrastructure and processes, and the need for radical changes to transition toward more sustainable systems. On one hand, materials must be somewhat compatible with current production and recycling capabilities to ensure economic feasibility and immediate scalability. On the other hand, breakthrough innovations often require a complete redesign of industrial systems and supply chains to fully realize the benefits of circularity. This section explores the challenges in material innovation, focusing on the need for advanced recycling techniques and the incorporation of Safe and Sustainable by Design (SSbD) principles.

Development of Sustainable Materials

The development of sustainable materials, such as CO_2-derived or bio-based alternatives, are essential for the circular economy. However, these materials often face challenges in meeting the performance standards of traditional materials and achieving economic viability at scale (earning trust of market). Real-time analytical techniques and chemical sensing are critical for assessing properties like stability, recyclability, and compatibility with existing processes. This ensures that sustainable materials meet both performance and circularity goals. Studies showing that these materials can outperform traditional ones in any substantial way (durability, safety, economy or recyclability for example) are key to driving their adoption. Establishing industry-wide standards is also necessary to ensure these materials are safe, durable, and recyclable while aligning with circular economy practices.

Advanced Recycling Techniques

Advanced recycling techniques are key to unlocking circularity, but significant challenges remain in ensuring the quality and safety of recycled materials. One critical issue is the presence of contaminants introduced during the product lifecycle (such as Non-Intentionally Added Substances (NIAS)) that can compromise the purity of recyclates. While current in-depth characterization methods provide valuable insights into these contaminants in laboratory settings, the challenge is to integrate this knowledge with online or at-line sensing technologies for real-time, on-site decision-making. In which case can we clean the bulk and when is going to monomer/dissolved-polymer optimal for decontamination, material properties and economy? Bridging this knowledge gap is crucial for implementation and improving the quality of recycled materials while ensuring their safe reuse in production cycles.

Another challenge lies in optimizing online sorting analytics. Although real-time sensors and AI-driven systems can enhance the sorting of materials by composition, the precision needed for high-quality recycling still requires significant improvement. Implementing reliable, real-time analytics that can operate efficiently in industrial settings is essential for reducing contamination and ensuring that recyclates meet the standards for reuse in circular production processes.

3.4 SSbD in Material Development

The Safe and Sustainable by Design (SSbD) framework is a cornerstone for embedding safety, sustainability, and circularity into the transitioning sectors this roadmap revolves around, and may be most prominent for chemical processes and biotechnologies. However, a critical challenge lies in the reliance on predictive tools and computational models. While these tools are valuable for planning and forecasting material behavior and potential risks, they have inherent limitations. For example, impurities and degradation by-products are rarely accounted for, despite their potential to emerge during production, use, or recycling. These substances may pose unforeseen risks to human health and the environment, leading to regrettable substitutions. This challenge is particularly pressing for materials designed to support circularity, as their performance and safety must be maintained across multiple use cycles.

To address these gaps, suitable analytical and sensing methodologies must be implemented early in the SSbD R&D phase and integrated throughout the entire lifecycle of materials. The recycling of plastics offers a clear example of how the absence of integrated, standardized, and cost-effective analytics can impede progress. Such a gap can foster a “best-not-to-know” mentality, where a reluctance to investigate certain risks hinders transparency and public trust. To prevent similar pitfalls in future material innovations, the requirements for SSbD analytics and sensing technologies need to be discussed and defined so the research community can deliver the required innovations in time.

Developing harmonized analytical requirements, metrics, and methods for assessing material safety and sustainability will establish a solid foundation for the successful implementation of SSbD. Collaboration between industry, academia, and regulators is essential to ensure these standards address the needs of all stakeholders. Analytical and sensing considerations must become integral to SSbD projects to provide robust data for informed decision-making. Additionally, these standards must align with existing regulatory frameworks and international guidelines to facilitate widespread adoption and compliance while safeguarding consumers and the environment.

3.5 References

[1]: National Circular Economy Programme | 2023 - 2030

[2]: Circular economy action plan - European Commission (europa.eu)

[3]: Safe and sustainable by design - European Commission (europa.eu)

[4]: KIA Circulaire Economie 2024-2027 | Publicatie | Topsectoren

[5]: KIA Key Enabling Technologies

4. Digital Chemistry

4.1 Introduction

The transformative impact of Artificial Intelligence (AI) on society can hardly be overstated, with AI-driven applications pervading sectors such as business and industry, government, education, entertainment, healthcare, and science. It has been estimated [1] that AI could enable the accomplishment of 134 out of the 169 defined targets across the 17 UN Sustainable Development Goals. By defining a separate Knowledge & Innovation Agenda (KIA) for Digitalization, the Dutch government has made digitalization/AI a prominent member of the Knowledge & Innovation Covenant (KIC) 2024-2027 [2]. Furthermore, digitalization and AI are strongly represented in the recently presented National Technology Strategy [3] and in the policy-shaping report “Growth markets for The Netherlands” [4].

For the Chemistry sector, AI tools and applications are being researched, developed, and deployed at a rapid pace, yet the AI revolution is only getting started [5]. This is mainly because the machine learning (ML) tools that underly AI applications need large volumes of accurate and accessible training data. In chemical domains where large training sets are readily obtained, such as analytical chemistry and biochemistry / molecular life sciences, AI is further along the Hype Cycle for Emerging Technologies [6] than other chemistry domains. This is reflected by the reported differences in growth of AI-related journal publications and patents for different chemistry subfields [7].

Considering the increasing importance of digitalization and AI in both public and private organizations in the Chemistry sector, this chapter of the CSET roadmap 2024-2027 is specifically focused on Digital Chemistry. This chapter is divided into the four tasks shown in Figure 4. An overview of the short-, medium-, and long-term goals within each task is provided in Table 7.

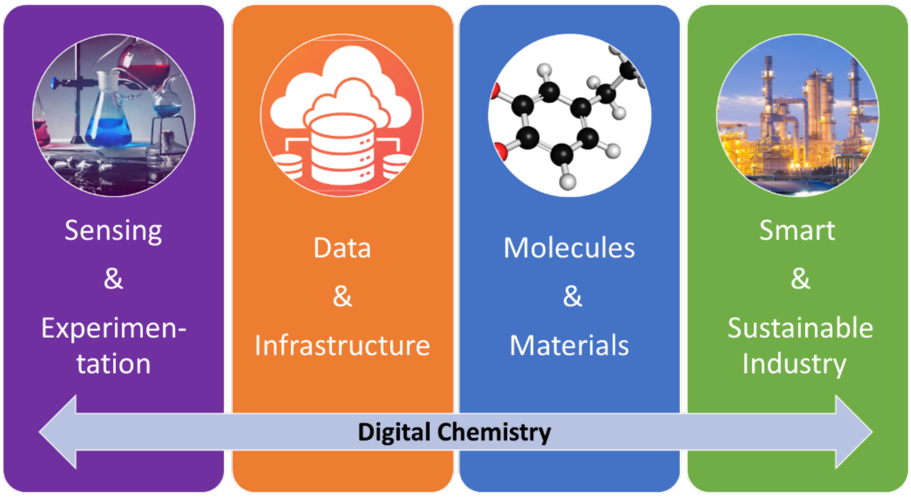

Figure 4: *Digital Chemistry topics covered in this chapter.*

Table 7: *Digital Chemistry tasks and their goals.*

Task	Short term goals now – 2030	Medium term goals 2030 – 2035	Long term goals 2035 – 2040	Ambition
Sensing & Experimentation	• Improved ML methods for analyzing large, multivariate, and multimodal analytical datasets • Development of in-/on-line analytics for high-throughput experimentation (HTE) • Methods for AI-assisted optimization of chemical experimentation	• Infrastructure for HTE coupled to in-/on-line analytics and AI available in NL and accessible to a variety of stakeholders • Successful use cases of HTE + analytics + AI in different application fields	• "Self-driving" labs widely implemented in knowledge institutes and industry	NL will be a major player and technology provider in AI-driven autonomous chemical experimentation
Data & Infrastructure	• Identification of analytical technologies necessary for a future proof chemistry • Standardization and harmonization of data and metadata collection • Development of automated data quality assessment approaches	• Building the ICT infrastructure for the data ingestion, storage, and reuse • Development of advanced data fusion technologies for leveraging the archived data	• Nation-wide deployment of the developed infrastructure in both knowledge institutions and industry	Having nation-wide infrastructure to facilitate data archiving and reuse for chemical analysis and discovery
Molecules & Materials	• Improved models for property and	• Widespread use of generative AI	• Safe and Sustainable by Design (SSbD)	NL will be a major driver for AI-enabled discovery of

	activity prediction • ML models for measurability assessments	for designing new molecules and materials • AI-enhanced models for long-term sustainability assessment of chemicals	development of molecules and materials is driven by AI	new and sustainable molecules and materials
Smart & Sustainable Industry	• Widespread implementation of Digital Twins for chemical manufacturing • Successful hybrid models for chemical process engineering	• Successful applications of (pilot) chemical plants running on Quality-by-Design models • AI-assisted design of chemical processes and plants	• Industry 5.0 technology (incl. process sensors, AI) fully developed and implemented in new chemical manufacturing and recycling plants	In chemical industry, NL will have and deploy the most efficient, safe, and sustainable manufacturing processes enabled by AI

4.2 Sensing and Experimentation

The combination of automation, robotics, chemical sensing/analysis and (generative) ML/AI is starting to revolutionize the field of chemical experimentation, as evidenced by a recent (2024) comprehensive overview about Self-Driving Laboratories (SDLs) published in Chemical Reviews [8]. Notable application areas include chemical reaction optimization (arguably the most widespread application of SDLs so far), drug discovery and bioengineering, and the design and optimization of materials (e.g. structural, optoelectronic and energy storage materials). For many SDL applications, the ability to chemically characterize samples on-line and in real time is crucial to maximize the efficiency of the automated synthesis or formulation system and provide the ML/AI algorithms with data in a fit-for-purpose manner (with respect to amount, quality, and timely availability of data). For example, the recently reported RoboChem platform based on flow chemistry for photocatalysis applications heavily relies on on-line benchtop NMR for chemical characterization [9]. Automation coupled to ML/AI also provides opportunities for optimizing chemical analysis methods themselves [8], [10].

AI-enhanced sensing / chemical analysis

With the increasing rate at which chemically-relevant raw data is being produced in laboratories and in the field (e.g. a chemical factory, a river, the atmosphere, or a human patient), the need for development and application of multivariate analysis tools (chemometrics/ML/AI) to convert raw signals into actionable chemical information becomes ever more important. Hence, improved methods for analyzing large, multivariate, and multimodal analytical datasets will continue to be needed in order to improve the chemical, spatial, and temporal resolution of chemical characterization and sensing systems. Relevant technique areas include spectroscopy (NMR, IR, NIR, Raman, UV-VIS, fluorescence, etc.), spectrometry (MS, atomic), separation science (also hyphenated with MS or other detectors), microscopy and imaging, and sensors based on other physical principles (e.g. ultrasound, density, etc.). For example, handheld or on-line spectroscopy systems for lab-to-the sample applications are increasingly integrated with cloud-based calibration or classification models that convert the measured spectroscopic signal into chemical concentrations or classification results. From this information, evidence-based decisions can be made (e.g. sorting plastic waste for recycling applications, or adjusting manufacturing process settings to optimize output quality).

AI-enhanced experimentation

To maximally benefit from the opportunities of AI-enhanced chemical experimentation, a tight integration must be developed between i) (high-throughput) hardware for synthesis, formulation, and/or (additive) manufacturing, ii) monitoring (often on-/in-line chemical analysis but can be different responses), and iii) ML/AI-based optimization and control software. Development of all these components and their integration into SDL solutions for relevant application fields in the Dutch chemistry landscape is stimulated.

Developing strategies for experimental planning in SDLs is a very active research field, with Bayesian Optimization proving to be a very common and successful strategy that aims to optimize some black-box function (for example a measurable chemical property) as a function of controllable experimental parameters. Progress in this area is driven by published software libraries that are often being made open-source, which facilitates adoption of successful algorithms by the research community and fosters collaboration.

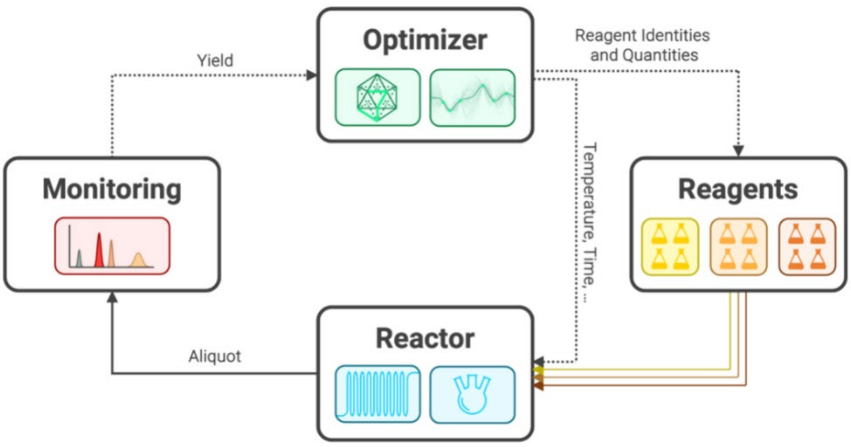

Figure 5: *General components of a closed-loop system for reaction optimization. Source: Ref. [8].*

4.3 Data and Infrastructure

Digital transformation and sustainable infrastructure are critical for future-proofing the field of chemistry, particularly analytical chemistry. These transformations will ensure that chemical research, development, and manufacturing are efficient, safe, and environmentally friendly. The adoption of digital technologies, such as artificial intelligence, big data analytics, and the Internet of Things (IoT), opens new research and development areas while enabling the chemical industry to optimize processes, reduce waste, and enhance productivity. By integrating digital tools, chemists can streamline experimental workflows, improve predictive modeling, and accelerate the future proof chemical discovery. The ability to simulate and optimize chemical reactions/processes digitally will result in more sustainable practices minimizing the negative impact of chemicals on the environmental and human health. Ultimately, such infrastructure will facilitate collaboration and data sharing within/between industries and across the global scientific community, fostering innovation and accelerating the transition to greener and future proof chemistry.

Harmonization of data and meta-data collection (data sharing and reuse)

The harmonization of data and metadata collection is a crucial aspect of the digital transformation to ultimately build a sustainable and future proof infrastructure for analytical chemistry community. In the context of digital transformation, harmonization involves the standardization of data formats, protocols, and metadata descriptors across various experimental setups and data sources. This will ensure that data generated from different analytical measurements can be seamlessly analyzed, compared, and shared, providing the means for greater collaborations and innovations. Harmonization and standardization of metadata collection will allow researchers to understand/assess the provenance, quality, and conditions under which data was collected. This knowledge is essential for accurate interpretation, further analysis, and ultimately integration of such data. By ensuring that metadata is comprehensive and standardized, data becomes more valuable and reusable, thus close to chemical information, enabling other researchers to replicate studies or apply the data to new hypotheses without ambiguity.

Infrastructure building for data storage and reuse

Analytical chemistry increasingly relies on complex data sets generated through high-throughput techniques. Storage and archiving of the collected analytical data become crucial to enable effective data sharing and reuse, minimizing redundant efforts and enhancing the reproducibility of experiments. This will be possible by building robust infrastructure for data storage and reuse. Developing robust, scalable data storage systems ensures that vast amounts of complex analytical data—such as spectrometric, chromatographic, and imaging results—are securely archived, retrievable, sharable, and analysable. Cloud-based solutions, including centralized databases enable seamless data sharing and integration across research teams and institutions, facilitating collaborative projects. A consequence of such harmonized platforms is the *a priori* implemented advanced data management plans including the data history. Such an infrastructure not only improves the existing research workflows by reducing redundancy but also accelerates the new discoveries and insights into a future proof chemistry.

Data fusion technologies

Data fusion, a process of integrating multiple data sources, for example different analytical technologies, enables the discovery of additional underlying trends in the data. Data fusion, when possible, has proved to be beneficial in gaining a more holistic view of the system, which is essential to a future proof chemistry and analytical chemistry. For instance, combining data from mass spectrometry, chromatography, and spectroscopy can lead to more accurate and reliable chemical identification and quantification. Also, coupling of process data to chemical analytical data will yield more and more information on how to optimize chemical processes as well as define novel more sustainable processes. The future proof digital transformation harmonization frameworks and the data storage/sharing platforms will pave the way for new developments in data fusion techniques as well as accelerating the pace of scientific discovery.

4.4 Molecules and Materials

Safe and sustainable (i.e. future-proof) molecules and materials are fundamental to human existence. The design of these new molecules and materials is based on their potential toxicity, environmental impact, and their use of resources throughout their lifecycle—from production to disposal. Prioritizing the safety and sustainability of chemicals will result in a reduced human chemical footprint, minimizing risks to human and environmental health.

Predictive models for property and activity prediction

Machine learning-enhanced Quantitative Structure Activity (QSAR) models represent a significant tool for future proof chemicals. Several properties and activities, including measurability, can accurately be predicted via trained and optimized ML models based on existing data. Recent developments in ML technology such as deep learning, active learning, or graph neural networks have resulted in improved predictive power and generalizability of QSAR models, enabling the identification of future proof chemical alternatives. Additionally, these models are able to identify the chemicals with high levels of prediction/measurement uncertainty, warranting further studies. The integration of ML in property/activity modeling accelerates the development of future-proof solutions, reducing the ecological footprint of chemical processes and enhancing public health protection.

Generative AI for design of new molecules and materials

Recent advances in generative models have offered a great potential for designing future-proof chemicals while maintaining functionality. These models mainly consist of Generative Adversarial Networks (GANs) and Variational Autoencoders (VAEs) and can generate novel chemical structures with desired properties and activities by learning from existing chemical data. Incorporation of safe and sustainable by design criteria into such models will result in inherently safe and future-proof chemicals. These models allow the exploration of a vast chemical space, uncovering solutions that conventional methods may overlook. Consequently, these models are able to drive the efficient development of next-generation chemicals that support sustainable industrial practices and environmental/human health protection.

AI enhanced environmental digital-twins for long-term sustainability assessment of chemicals

AI-enhanced environmental digital twins or fate models are crucial for the long-term sustainability assessment of chemicals. These models provide dynamic and real-time simulations of chemical interactions with soil, water, and air, to accurately forecast its fate and behavior on different time scales. These models create detailed scenarios that mimic the life cycle and environmental impact of chemical substances. By continuously learning and adapting to new data, these AI-enhanced models can forecast potential ecological consequences, optimize chemical usage, and identify safer alternatives. Furthermore, these modeling strategies facilitate stakeholder involvement by providing transparent, data-driven insights, resulting in informed and proactive decision-making. Ultimately, these models can foster the development of sustainable chemical practices to protect human and the environmental health.

4.5 Smart and Sustainable Industry

Production processes in the (petro)chemical, agro/food, pharmaceutical and other manufacturing industries are heavily monitored by sensors in order to ensure the safety and efficiency of the process. Traditionally, in-process sensors are mostly used for monitoring physical parameters such as temperature, pressure, flow, density, etc. However, chemically specific measurements are nowadays being adopted for process monitoring as well in order to provide more detailed chemical information about the process, which in turn further enhances process understanding and enables improved process control. Process Analytical Technology (PAT) tools and applications based on, for example, in-/on-line chromatography techniques (GC, LC) or spectroscopic techniques (e.g. near-infrared (NIR), Raman, and UV-VIS) are increasingly developed and implemented in chemical processes for this purpose. For production processes using raw materials with high variability such as recyclates and bio-based materials, the need for better process monitoring and characterization of raw material complexity becomes even more important.

Table 8: *Example application areas of ML/AI (often in combination with physics-based models) for chemical engineering.*

Process design & understanding	• Parameter/property prediction (thermodynamics, kinetics) • Unraveling reaction mechanisms • Hybrid models for flow dynamics and transport • P&ID design • Operator training using modules from historical plant data
Condition monitoring & digital twins	• Predictive maintenance • Fault/anomaly detection • Hybrid (data-driven and physics-based) modeling for digital twins
Process control & optimization	• Model-predictive control • Reinforcement learning • Real-time optimization
Predictive models for quality	• Soft sensors • Discrepancy models • Iterative learning • Uncertainty quantification
Scheduling	• Production scheduling & planning • Supply chain optimization

ML/AI methods provide great opportunities for boosting developments in many aspects of chemical engineering, as exemplified in recent reviews [11], [12]. R&D efforts and (pilot) plant scale implementations are stimulated for application areas shown in Table 8.

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5. Health & Care

5.1 Introduction

The central mission of the Dutch healthcare innovation policy for 2040 (as presented in the Knowledge and Innovation Agenda "Health & Care") is (1) to enable all people in the Netherlands live on average at least 5 years longer in good health compared to the current situation (2024), and (2) to reduce the health differences between the highest and lowest socioeconomic groups by 30%.

The twofold central mission is supported by five specific missions, which focus on (a) improving living environment and lifestyle, (b) providing care in the patient's home environment, (c) increasing societal participation of people with a chronic disease or disability, (d) improving the quality of life for people with dementia, and (e) protecting the population against health threats with a disruptive impact on society.

Chemical sensing and enabling technologies will play an important role in the realization of all missions. Society will benefit from CSET innovations, e.g. by the possibility of early diagnosis and self-monitoring. Personalized medicine and the possibility of targeted drug delivery will have a large impact on overall health and disease treatment, for example by reducing side-effects. At the same time, innovations in organ-on-chip will result in increased added value and reduced time to market of medication, and reduced animal testing. This combination of effects will contribute to the emergence of a more patient-centered and sustainable healthcare system, enabling people to live a longer and healthier life.

The CSET Health & Care roadmap is organized around two application areas (see Figure 6):

1. Detection and monitoring technologies - Point of care diagnostics and (continuous) monitoring of medical conditions and environmental parameters with a health impact (e.g. air quality) are enabled by biosensing and lab-on-chip technologies. Similar technologies also enable improved monitoring of drug production processes, resulting in higher production efficiency and higher quality of pharmaceutical and biological drugs.

2. Lab-on-chip technologies for in vitro living systems. Drug development can be accelerated and optimized by organ-on-chip technologies. Together with other enabling technologies, this could ultimately result in personalized treatment. Other applications of CSET technologies can be found in the fields of artificial organs and cell and tissue engineering.

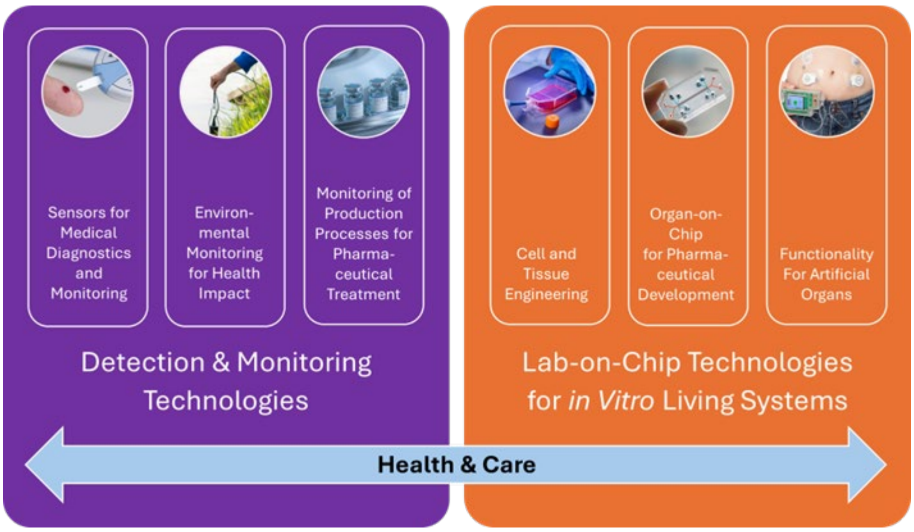

Figure 6: Health & Care topics covered in this chapter.

Table 9: *CSET tasks and goals in the application area Health & Care.*

Task	Short term goals now – 2030	Medium term goals 2030 – 2035	Long term goals 2035 – 2040	Ambition
Detection and monitoring technologies	• Environmental and production monitoring using biomarkers in the millimolar range • Biomarkers are measured near the patient (POCT = point of care testing, individual samples are taken and measured)	• Environmental and production monitoring using biomarkers in the micromolar range • Biomarkers are measured continuously, samples are automatically taken via a medical device, e.g. via a catheter (continuous monitoring)	• Environmental and production monitoring using biomarkers in the nanomolar and picomolar ranges. • Biosensors are worn on or in the body (wearable, ingestible, implantable)	Biosensors improve patient care, environmental monitoring, and the production of biopharmaceutical treatments
Lab on chip technologies for in-vitro living systems	• Devices for cell and tissue research • Expanded library of (single/combined) organ models on chip • Chemical sensing to monitor efficiency of future artificial organs	• Devices for cell and tissue research including integrated sensing technologies • Interacting organ models mimic complex body function (human-on-chip) • Portable artificial organ solutions	• Devices for cell and tissue diagnostics • Standardized platforms facilitate development of organ-on-chip applications • Partly implantable artificial organ functionality	Organ-on-chip devices accelerate drug development, enable precision/personalized medicine, and reduce animal testing Artificial organs will enable normal participation in society

5.2 Detection and monitoring technologies

Sensors for medical diagnostics and monitoring

The development and implementation of biosensing and lab-on-chip technologies in medical diagnostics and monitoring is a multidisciplinary challenge and requires close collaboration between experts from the fields of device technology, chemistry, biology, and clinical practice.

Biosensing and lab-on-chip technologies promise to provide faster and more accurate measurement data, resulting in earlier diagnosis, better treatment decisions, and improved patient outcomes. Potential embodiments of lab-on-chip technology include smart patches, smart fibers, smart probes, smart catheters, smart implants, etc. Advanced systems will combine and integrate sensing and actuation principles of physical and (bio)chemical nature.

Technologies should be developed to sense and control living systems in-situ and in real time, which would improve the added value of medication, therapy effectiveness and compliance, which in turn would reduce the overall healthcare costs through disease management and early detection of exacerbation.

Application examples are:

- Real-time sensing on the body or in the body
- Accurate drug administration using real-time data as an input
- Neuronal stimulation based on objective signals from the body and/or the environment
- Point of care diagnostics and monitoring (e.g. in personalized or precision medicine)
- Patient monitoring in critical care, e.g. inflammation monitoring and therapeutic drug monitoring
- Small biochemical sensors integrated into medical devices and disposables, which are in contact with the human body and continuously monitor the biochemical status of patients.
- Materials and devices for drug delivery and for bio-mimetic stimulation.
- Systems for comprehensive biochemical profiling. Systems for closed-loop monitoring and treatment.

Environmental monitoring for health impact

Our environment impacts our health every single day. Determining the impact on our environment, and implications for emitters, require much more detailed information from distributed chemical sensor systems to act on practices. NOx and ammonia, microplastics and particulate matter require novel methods to enable continuous monitoring due to significant challenges with long term accuracy, calibration, specificity, and deterioration of sensitivity over time. Early warning systems for air and water, (e.g. related to elevated levels of pesticides or drug waste) provides a use case where detecting sudden changes in concentration are sufficient without the need for accurate concentrations. To further enhance our understanding of environmental health impacts, emerging tools that measure toxicologically relevant factors (like the assessment of oxidative potential and environmental DNA) should be integrated into monitoring strategies.

Despite the attention for outdoor hazards, most of our exposure, even to outdoor air pollution, occurs indoors because of the time we spend there. Air quality monitoring, cleaning, and control indoors are therefore very relevant and dependent on chemical sensing functionality for a wide range of harmful substances (CO_2, VOCs such as BTX, bacteria and viruses, etc.).

Monitoring of production processes for pharmaceutical treatment

Industrial processes will benefit from novel measurement-and-control functionalities enabled by biosensors and lab on a chip technologies. For example, the monitoring of small molecules, proteins, and nucleic acids can improve cell-based production processes, for making biologicals, viral vaccines or stem cells for example. Sensors are needed for continuous monitoring of bioreactors (upstream processing) and of extraction and purification (downstream processing) for the manufacturing of innovative biopharmaceutical products.

In addition, chemical and biochemical research increasingly exploits fluidic microdevices for the synthesis of new compounds and for tailoring formulations to maximize the effectivity of the compounds. Microtechnologies and microfluidics allow for the synthesis of small amounts of high-value specialty products and allow controlled structure formation. Such technologies, for which further development is still needed, will enable the seamless upscaling from research to production (‘scalable flow chemistry’), which will be very helpful for the emerging paradigm of precision medicine and for innovations in nutrition.

Application examples are:

- Microfluidic technologies for the synthesis and control of new active pharmaceutical ingredients (e.g. biologics by enzymatic cascade reactions in multiphase flow systems)
- Development of encapsulates for targeted compound delivery with sustained activity ('formulation'). This approach is valid for medication as well as for other sectors such as food, personal care, etc.
- Integrated and flexible production processes of formulated drugs.

5.3 Lab on chip technologies for in-vitro living systems

Cell and tissue engineering

Tissue engineering combines cells, scaffolds, and growth factors to regenerate tissues or replace damaged or diseased tissues, while regenerative medicine combines tissue engineering with other strategies, including cell-based therapy, gene therapy, and immunomodulation, to induce in vivo tissue/organ regeneration. Lab on a chip technologies are needed for the next generation of solutions in the fields of cell and tissue engineering. For example, novel sensors to enable the continuous monitoring of bioreactors (upstream processing) and of extraction and purification (downstream processing) for the manufacturing of innovative biopharmaceutical products, such as stem cells.

Laboratory-grown cells and tissues can be injected or implanted to stimulate the body's own repair mechanisms, which is the premise of the field of regenerative medicine [1]. Such complex applications require close collaboration between device technologists and cell biologists in order to develop lab on a chip technologies that solve pressing needs in research.

Organ-on-chip for pharmaceutical development

The development of novel pharmaceutical compounds is inherently complicated by the complexity of the human body and the variability between people. Furthermore, for ethical reasons the testing of new pharmaceutical compounds on animals and humans should be minimized (cosmetics testing on animals has already been forbidden in the EU since 2013).

This calls for the development of tissue, organ, and multi-organ human model systems on a chip. Such model systems (known as organ-on-chip systems) can support scientific research on how the human body works and can help to improve and accelerate the testing and development of novel pharmaceutical compounds [2, 3].

Building on organ-on-chip platforms, personalized model systems are envisioned to become available in the future. These could for example be built from induced pluripotent stem cells (iPSC technology), which allow creating functional tissues and organs on a chip, which possess the genetic (disease) profile of the patient and thus allow the realization of precision or even personalized medicine. Ultimately, this could result in multi-organ model systems, culminating in a so-called 'human-on-a-chip'. However, despite the progress in recent years, there are still numerous biological, technological, and economical challenges to be solved before organ-on-chip systems can realize their full potential.

The scope of the CSET roadmap Health & Care covers the development of new sensing and enabling technologies for organ-on-chip applications that accelerate the discovery, development, and implementation of the next generation of pharmaceuticals and reduce the use of laboratory animals. This includes the development of new measurement methods to improve the safety and efficacy of therapies. Applications of such organ-on-chip systems may include the development of drugs to treat dementia, vaccines or medicine to cope with societal health challenges, and cellular and genetic therapies.

Functionality for Artificial organs

Artificial organs replace (parts of) organ functionality. The Dutch Dr. Willem Kolff (inventor of the artificial kidney and artificial heart) internationally is regarded the “Father of Artificial Organs”. A recent success is the wearable dual-hormone artificial pancreas of INREDA (2024 Kolff Prize winner) and the Dutch Growthfund NXTGEN supports further miniaturization towards smart implantable artificial organs. Although fully implantable artificial organs still require long timelines, modular subsystems already show promising results. A good example is chip-based removal of Protein-Bound Uremic Toxins (PBUTs) from the blood of dialysis patients, which requires chemical sensing to monitor efficiency over time and eventually needs to support closed-loop control. It is clear that many lessons learned in the Organs-on-Chip domain can be re-used for Artificial Organs.

Over the next decade, improvements in such technologies aim to first enable patients to receive treatment at home, then transition to portable solutions, and eventually receive (partly) implantable care. With each step, participation in society becomes increasingly self-evident, “taking the patient out of the person”, one step at a time.

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6. Industrial Safety and Process Development

6.1 Introduction

CSET-relevant key technologies such as advanced analytics and sensoring, data science and modelling, and flow chemistry will play a crucial role in developing new processes and improving the monitoring and control in the (petro)chemical, agro/food, and pharmaceutical industries. Applications of improved and extended sensing in the processing industries will benefit both design of new processes (e.g. by improving chemical understanding) and the efficiency and sustainability of processes at plant-scale, but also their safety aspects. To implement "Factory of the Future" and "Industry 5.0" concepts in practice (see also the section Smart Sustainable Industry in the chapter Digital Chemistry), developments in key CSET technologies are therefore needed and proposed in this chapter. An overview of tasks and their goals for Industrial Safety and Process Development is provided in Table 10.

Table 10: *Industrial Safety and Process Development tasks and their goals.*

Task	Short term goals now – 2030	Medium term goals 2030 – 2035	Long term goals 2035 – 2040	Ambition
Industrial Safety	• Wearable, portable, or fixed sensors for rapid and highly sensitive air monitoring of specific chemicals of concern in a production environment, including ATEX zones • Handheld rapid identity testing of raw materials to prevent chemical misoperations • Standoff portable sensors for rapid identification of leaked chemicals (e.g. liquids, solids) in a plant or in the environment	• Drone-based miniaturized sensors for environmental surveillance of chemicals, e.g. in case of inadvertent release or leakage • In-/on-line process analytical technology that completely avoids manual sampling from a process pipeline or reactor • In-/on-line sensing techniques, including soft sensors, that provide early warning signals for potentially hazardous	• Full integration of chemical sensing networks and AI/ML-assisted process monitoring and control across the (petro)chemical, agro/food and pharmaceutical industries	The Dutch chemical sector serves as a global example for Industrial Safety

		process deviations or upsets		
Process Development	• Novel multi-modal process analytical technologies with improved chemical, spatial, and temporal resolution. • Availability of miniaturized in-/on-line detection technologies for in situ measurement of reactants, intermediates, and products and catalyst behavior at different time and length scales	• Availability of innovative micro-flow reactor technologies for gas-, liquid- and solid-phase chemistries • Improved chemical process understanding and control through chemical sensing coupled with advances in modelling (incl. DFT, process modelling and AI/ML)	• Implementation of the “Factory of the Future” on the basis of flow chemistry in a variety of chemical production processes	Dutch R&D and industry is a frontrunner in innovative chemical process design and development

6.2 Industrial Safety

Industrial manufacturing operations must be organized, managed and executed in such a way that employees and assets are protected by minimizing hazards, risks, and accidents. Whereas employee behavior, company culture, and HSE regulations are major drivers for a safe industrial environment, there are technological opportunities and challenges related to CSET that will contribute to the enhanced safety of both the occupational and process/production aspects of future manufacturing. The term “Safety by Design” is at present an integral part of the European “Joint Technology Initiative” SPIRE, recognizing the importance to consider safety as an integral part of industrial design. To this end, chemical sensors and advanced enabling technologies with high specificity and improved sensitivity must be developed for fixed deployment both in and around a production process as well as for flexible use by operators in a plant environment.

The main challenges related to sensing for industrial safety are i) the development of new and/or improved sensing mechanisms for chemically specific detection and ii) turning such sensing mechanisms into low-cost, rapid, robust, small and sensitive physical sensors. This will require tight collaboration between research groups and instrument developers and vendors (e.g. high-tech SME or larger vendors). A particular additional challenge is the development of sensors that work robustly in chemically demanding (e.g. corrosive, ATEX) environments.

With the growing importance of artificial intelligence (AI)-based process control mechanisms also comes an increased reliance on data quality, which means that sensors and their data must be(come) highly reliable and robust.

6.3 Process Development

Processing industries are under continuous pressure to maintain or increase their competitiveness in terms of economic efficiency, sustainability, flexibility, and safety. To address this challenge, it will be crucial to rapidly and effectively design and scale up new and improved processes (Factory of the Future). In turn, this will fuel the need for a more fundamental understanding of raw material characteristics (which, increasingly, are complex bio-based materials), (bio)chemical pathways and their corresponding thermodynamics. Flow chemistry will have important added value in this regard by its ability to translate processes at nano- or micro-scale to those at pilot plant scale.

Key in achieving the vision for the "Factory of the Future" using flow chemistry are smart analytical (nano)technologies which can create a more detailed understanding of chemical pathways and which are anticipated to be also applicable for larger scale flow chemistry. In general, the availability of in-/on-line analytical technologies will enable the characterization of chemical reactions and their catalysts at the spot, without time delay and without sampling demand or any other interference to the spot of information. Such developments in Process Analytical Technology (PAT) will become key enablers for realizing smart process control systems as envisioned by the Industry 5.0 platform. PAT sensors can be integrated into bigger modern process control systems. Thus, the sensors and derived new process control concepts can lead to a unification of the formerly different and separate stages and thereby lead to massive shortening of process development time. This is to go hand in hand with bringing in advanced molecular modelling (including density-functional theory (DFT)) and process modelling approaches for improving our understanding of chemical processes and the way that such processes can be controlled. Also, the increased interest in gas- and solid-phase flow chemistry is of importance and opens a new window in micro-reactor engineering, process modelling, phase separation (down-stream processing) technologies, and dedicated analytical technologies.

Apart from the search and implementation of new complex chemical processes, the increasing expectations from customers on product quality and the need for ultimate reliability of the complete production processes are regarded as decisive challenges. As an example, manufacturing of polymer-based biomaterials and chemically modified biopharmaceuticals will face ever-increasing quality demands from regulatory bodies, also putting great emphasis on process reliability.